soft-gelatin capsule form, e.g. compositions prepared in accordance with the preceeding examples 1 through 4 or 6 or 7.

STUDY II

Groups of 8 beagle dogs (male, ca. 11–13 kg) are used. Animals receive no food within 18 hours of administration of test composition but are allowed free access to water until administration. Test composition is administered by gavage, followed by 20 ml NaCl 0.9% solution. The animals are allowed free access to food and water three hours after administration of test composition.

2 ml blood samples (or 5 ml for the blank) are taken from the vena saphena and collected in 5 ml plastic tubes containing EDTA at −15 min. (blank), 30 min., and 1, 1.5, 2, 3, 4, 6, 8, 12 and 24 hours post administration. Blood samples are stored at −18° C. pending assay.

Blood samples are analysed by RIA. Areas under the blood drug concentration versus time curves are calculated by the trapezoidal rule. Analysis of variance is performed with respect to AUC (area under curve), Cmax (maximum concentation) and Tmax (time of maximum). Calculated average AUC (in ng hr./ml^{-1}) and Cmax (in ng/ml^{-1}) values from individual trial runs together with calculated variation in response between test animals receiving the same test composition (CV), demonstrate high bioavailability (AUC and Cmax.) coupled with relatively low variability in subject response both for AUC and Cmax for compositions in accordance with the invention, e.g. in accordance with example 6 above, as compared e.g. with results for the known SANDIMMUN CYCLOSPORIN A drink solution composition (e.g. as described in relation to the following CLINICAL TRIAL) administered at the same Ciclosporin dosage level.

CLINICAL TRIAL

The advantageous properties of the compositions of the invention on oral administration may also be demonstrated in clinical trials, e.g. performed as follows:

Trial subjects are adult volunteers, e.g. professionally educated males of from 30 to 55 years. Trial groups suitably comprise 12 subjects.

The following inclusion/exclusion criteria are applied:

Inclusion: Normal screening ECG; normal blood-pressure and heart rate; body weight=50–95 kg.

Exclusion: Clinically significant intercurrent medical condition which might interfere with drug absorption, distribution, metabolism, excretion or safety; symptoms of a significant clinical illness in the two-week pre-trial period; clinically relevant abnormal laboratory values or electrocardiogram; need for concomitant medication during the entire course of the study; administration of any drug known to have a well-defined potential toxicity to a major organ system within the previous 3 months; administration of any investigational drug within 6 weeks prior to entry into the trial; history of drug or alcohol abuse; loss of 500 ml or more blood within the past 3 month period; adverse drug reaction or hypersensitivity; history of allergy requiring drug therapy; Hep.-B/HIV-positive.

Complete physical examination and ECG is performed pre- and post-trial. The following parameters are evaluated within 1-month periods pre- and post-trial:

Blood: - red blood cell count, haemoglobin, hematocrit, erythrocyte sedimentation, white blood cell count, smear, platelet count and fasting glucose;

Serum/plasma—total protein and electrophoresis, cholesterol, triglycerides, Na^+, K^+, Fe^{++}, Ca^{++}, Cl^- creatinine, urea, uric acid, SGOT, SGPT, alkaline phosphatase, total bilirubin, α-amylase; Urine—pH, microalbumin, glucose, erythrocytes, ketone bodies, sediment.

Creatinine clearance is also determined 1-month prior to trial entry.

Subjects each receive trial compositions in randomised sequence. Compositions are administered orally, once to a total dose of 150 mg cyclosporin, e.g. Ciclosporin, and at least 14 days are allowed between each administration.

Administration is performed in the morning after an overnight fast of 10 hrs. with only water allowed. Only caffein-free beverages are permitted within the 24 hr. period following administration. Subjects are not allowed to smoke within the 12 hr. period following administration. Subjects receive a standardised lunch 4 hrs. following administration.

Blood samples (2 ml) are taken 1 hr. prior to administration and post-administration at 0.25, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 6, 9, 12, 14, 24, 28 and 32 hrs.. For determination of creatinine 2 ml blood samples are taken immediately prior to administration and at 12, 24 and 48 hrs. post-administration. Samples for cyclosporin determination are collected in two EDTA coated polystyrene tubes (1 ml each) at each time point and are deep frozen at −20° C. after gentle agitation. Cyclosporin is assayed in whole blood using RIA with specific and/or non-specific MAB assay—detection limit in both cases =ca. 10 ng/ml.

In trials carried out in accordance with the above protocoll, e.g. comparing the composition of example 6 in hard gelatin encapsulated form with the current Ciclosporin drink solution (Ciclosporin=50 mg, LABRAFIL=150 mg, ethanol=50 mg, maize oil=213 mg, in soft gelatin encapsulated form: content end weight=463 mg/dosage) as standard, substantially increased bioavailability levels for the example 6 composition are recorded in comparison with the standard as reflected in both AUC (0–32 hrs) and Cmax values established. In addition, comparison of variation in whole blood Ciclosporin concentration (as determined by specific monoclonal RIA) with time following single administration of test compositions to a Ciclosporin dosage of 150 mg, demonstrates marked reduction in variability of response between all subjects receiving composition in accordance with example 1 as compared with that for all subjects receiving the standard composition.

Similar or equivalent results may be obtained following oral administration of other compositions in accordance with the invention, e.g. as herein described in examples 1 through 5 or 7.

I claim:

1. A pharmaceutical composition for oral administration comprising cyclosporin A as active ingredient in a carrier medium comprising a transesterification product of a natural vegetable oil with glycerol, wherein said transesterification product comprises a mixture of monoglycerides, diglycerides and triglycerides.

2. The composition of claim **1**, wherein said vegetable oil is selected from the group consisting of corn oil, almond oil, ground-nut oil, olive oil and palm oil.

3. The composition of claim **2**, wherein said vegetable oil is corn oil.

4. The composition of claim **1**, wherein the amount of monoglyceride is 35 to 50% by weight, based on the total weight of said transesterification product.

5. The composition of claim **2**, wherein the amount of diglyceride is less than 40% by weight, based on the total weight of said transesterification product.